

transplantation. In addition, no increase in CMV or EBV reactivations has been observed so far under the profound “innate control.” Up to date, none of the patients developed aGVHD > grade II.

Conclusion: ATG Busulfan Fludarabine is a low toxicity platform for abTCR-depleted transplantations, resulting in a swift reconstitution of innate cells (NK cells and gd T cells) the first 6 months post transplantation. This transplantation strategy can serve as a tool for future immunological interventions such as a pre-emptive DLI or transfer of genetically modified T cells.

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Role of Hematopoietic Cell Transplantation Co-Morbidity Index (HCT-CI) in Selection of Conditioning Regimen for Patients Undergoing Allogeneic Hematopoietic Cell Transplantation (Allo-HCT) – a Single Institution

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Objective: To compare Overall Survival (OS), Treatment Related Mortality (TRM), and Relapse Rate (RR) between myeloablative conditioning (MAC) and reduced intensity conditioning (RIC) regimens in patients with high/intermediate risk disease status. The hypothesis to be tested is that HCT-CI can be effectively used to decide on the preference of conditioning regimen and that RIC will decrease TRM without increasing relapse so that OS will be improved even in high/intermediate risk disease status patients with high HCT-CI.

Patients and Methods: Patients with high HCT-CI (≥ 3) underwent RIC regimen and those with low HCT-CI (≤ 2) underwent MAC regimen despite high/intermediate risk disease status. We analyzed the outcome of 92 patients with high or intermediate risk disease status (CIBMTR criteria) who underwent Allo-HCT at our institution between the years 2009 and 2013 inclusive. RIC regimen consisted of IV Fludarabine 30mg/m²/day infused over 30 minutes for 5 days on days -6 through -2 and IV Busulfan 3.2 mg/kg/day on days -3 and -2 (infusion rate 80 mg mg/hour). MAC regimen consisted of IV Fludarabine 50mg/m²/day infused over 1 hour on days -6 through -2, IV Busulfan 3.2mg/m²/kg/day on days -5 through -2 (infusion rate 80mg/hr), and TBI 200 cGy on days -2 and -1. All patients received Thymoglobulin at a total dose of 4.5 mg/kg or 6 mg/kg administered in divided doses on days -2, -1 and 0. Post-transplantation graft versus host disease (GVHD) prophylaxis consisted of tacrolimus and mycophenolate mofetil. Diagnoses included Acute Lymphoblastic Leukemia (n=4), Myeloproliferative disorder (n=7), Hodgkin's Lymphoma (n=8), Myelodysplastic Syndrome (n=20), Acute myeloid leukemia (n=25), and Non-Hodgkin's Lymphoma (n=28). Median age of the recipients was 52.1 years. The HCT-CI was high (≥ 3) in 41 recipients (47%) and 75 patients (83%) were in high risk disease status.

Results: At a median follow up of 13.2 months, the OS for patients undergoing RIC was 74.3% compared to 38.1% with MAC ($p=0.014$). The cumulative incidence of TRM at 12 months was 27.6% in patients undergoing MAC compared to <1% in RIC ($p=0.041$). Relapse related mortality at 12 months in RIC (25.7%) compared to MAC (50.5%) was not statistically different ($p=0.206$).

Conclusion: Our data demonstrates that use of HCT-CI is a simple but effective way to appropriately stratify patients with high/intermediate disease risk status to a particular conditioning regimen. The use of RIC in patients with high HCT-CI is non-inferior to MAC with our institutional data showing RIC is associated with low TRM, improved OS

without any statistically significant increase in mortality from disease progression or relapse. Prospective studies are necessary to validate these findings.

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Outcomes of Allogeneic Hematopoietic Cell Transplantation (AHCT) for Multiple Myeloma (MM): Impact of Disease Risk and Conditioning Regimen

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Background: AHCT remains the only curative option for MM despite improved survival with novel agents. We analyzed our single center experience of AHCT in MM over the past decade and examined factors associated with outcomes.

Methods: The outcomes of 77 consecutive MM patients receiving allotransplants from matched sibling (n=69) or unrelated donors (n=8) between 2002 and 2013 at our institution were analyzed. The primary objectives were to compare overall survival (OS), progression free survival (PFS), and non-relapse mortality (NRM) in patients based on biologic disease risk and conditioning regimen intensity. 60 pts. received allotransplant after non-myeloablative regimens (regimen 1) – low dose 200-cGy total body irradiation (TBI) +/-Fludarabine (n=52) or Cyclophosphamide + Fludarabine (n=8) while 17 received higher intensity conditioning (regimen 2) consisting of Fludarabine + Melphalan 140 mg/2 (11) or Cyclophosphamide + TBI (6).

Results: Patient, disease and transplant related characteristics are given in Table 1. Median follow up of survivors was 49.4 months. 27 (35.1%) had high-risk cytogenetics – t (4:14), 17p deletion, Chr 1 abnormality, or t (14:16). 96% had prior auto transplant with 17(22%) relapsing after auto transplant.

On multivariate analysis, older age (HR 1.06 95% CI 1.015, 1.120, $p=0.0112$), lack of a complete remission (CR) at allotransplant (HR 0.15 95% CI 0.046, 0.485, $p=.0015$ in CR), longer interval from autologous transplant to AHCT (6.0 m vs. 5.2 m) (HR 1.04, 95%CI 1.008, 1.072, $p=0.01$) and CMV reactivation (HR 3.2, 95% CI 1.41, 7.52, $p=0.005$) were significant for higher mortality. CR at the transplant was associated with superior PFS (HR for treatment failure 0.332, $p=0.041$). Increasing age (HR, 1.07 $p=0.047$) and non-CR status at transplant (HR for CR - 0.164, 95% CI .035, .770, $p=0.021$) were associated with higher NRM. High-risk-disease and conditioning intensity were not associated with outcomes (Fig 1, 2).

Conclusions: The adverse effect of high-risk genetics may be overcome by the allogeneic effect irrespective of conditioning intensity. Allotransplant benefited younger patients and those in CR at the time of transplant and with short intervals from prior auto-grafts. No plateau in survival was demonstrated.

Table 1

Variables	Total, N=77	Regimen 1, N= 60	Regimen 2, N=17(%)	P value
Age, years median (range)	52(23–69)	52.5(32–69)	52(23–61)	0.40
Female, n (%)	28(36.4)	26(43.3)	2(11.8)	0.017
FISH risk, n(%)				0.55
Low	50(64.9)	40(66.7)	10(58.8)	
High	27(35.1)	20(33.3)	7(41.2)	
Time from auto to AHCT, months median (range)	5.2(3.3–75.2)	5.0(3.0–47.1)	6.3(4.1–75.2)	0.02
Response status at transplant,n(%)				0.21
CR	23 (29.9)	15 (25.0)	8 (47.1)	
PR	47 (61.0)	39 (65.0)	8 (47.1)	
SD	7 (9.1)	6 (10.0)	1 (5.9)	
CMV reactivation, n(%)	14 (18.2)	9 (15.0)	5 (29.4)	0.28

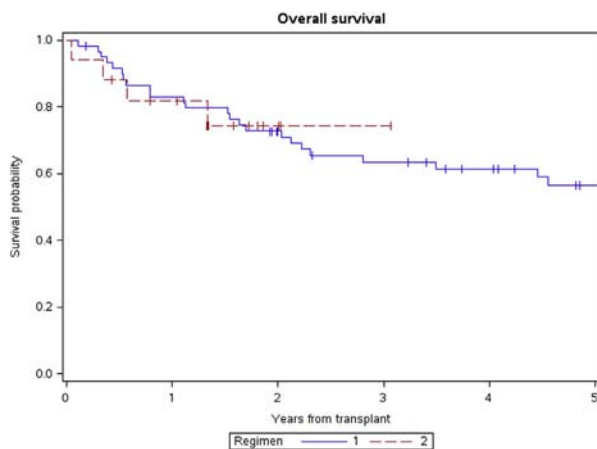


Figure 1. Overall survival by conditioning regimen intensity

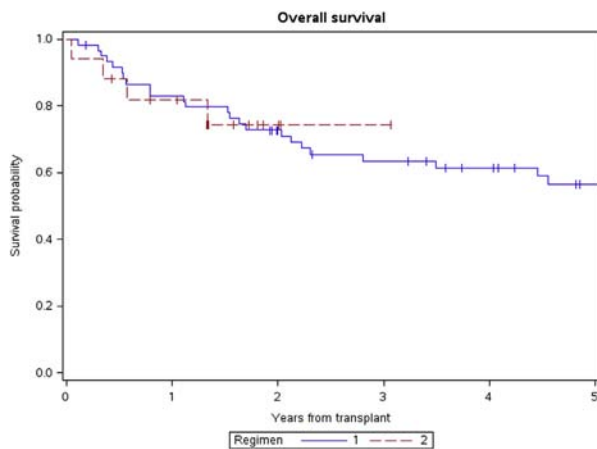


Figure 2. Progression free survival by FISH risk

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Background: Treatment with TKIs has greatly improved the outcome of patients with Ph+ALL. However most older patients are excluded from clinical studies, the curative potential of allogeneic hematopoietic stem cell transplantation (allo-HSCT) has not been fully analyzed. We examine the clinical features and transplant outcome of elderly Ph+ALL patients in the era of TKI.

Methods: We analyzed the data from 30 Ph+ALL patients aged 50 years or older who had used TKI before allo-HSCT.

Results: The median age was 59 years (range<r>: 50–71); 15 patients (50%) were older than 60 years. Subjects comprised 13 males and 17 females. The disease status at allo-HSCT was complete remission (CR) in 23 patients and non-CR in 7 patients. Before HSCT, 23 patients received imatinib-based chemotherapy, and 7 patients received dasatinib-based chemotherapy. The majority of the donors were HLA-matched unrelated (n=16) and related (n=6), followed by mismatched unrelated cord blood (n=7). Median follow-up for survivors was 247 days (r:16–4,156). The median HCT comorbidity index score was 1 (r:0–3). Median white blood cell count at diagnosis was $26.3 \times 10^9/L$ (r: 4.2–301.9 $\times 10^9/L$). Type of BCR breakpoint was minor in 23 patients (67%). Graft-versus-host-disease (GVHD) prophylaxis was calcineurin inhibitor-based in all patients (CsA:13 patients, FK506:17). Eleven patients received reduced-intensity conditioning regimens, nineteen patients received myeloablative conditioning regimens. The median duration from the diagnosis to HSCT was 197 days (95–763). No patient received TKIs after HSCT.

The probability of overall survival (OS) and disease free survival (DFS) at 1 year after HSCT were 46.0% and 42.0%, respectively. These results were not statistically different compared to the 35 patients aged under 50 years who had used TKIs before allogeneic HSCT. Multivariate analysis showed that the factor to influence OS was disease status (CR or nonCR) ($p=0.01$). Cumulative incidence of nonrelapse mortality (NRM) was 23.1% at 100 days after HSCT, and 52.0% at 1 year. The cumulative incidence of acute graft-versus-host disease <GVHD> (grade II–IV) and chronic GVHD at 1 year were 51.8% and 23.1%. Four patients relapsed after HSCT with a median of 329 days (r:112–475 days). The estimated cumulative incidence of relapse at 1 year was 8%. These outcomes (OS, DFS, NRM, relapse rate) were not significantly different when stratified by age groups (under vs. older than 60 years old). Increasing age was not associated with increases in acute or chronic GVHD. All of patients aged more than 60 years had HCT comorbidity index scores of ≤ 2 . Eighteen patients died at 139 days (r:16–1,219). The main cause of death was infection (10 patients).

Conclusion: Allo-HSCT for elderly Ph+ALL patients may be one of the promising strategy. Allo-HSCT would be effective option for carefully selected patients aged 60 or older with Ph+ALL.

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High Doses of Myeloid Progenitor Cells Induce Tolerance in the Context of Autologous HSC Transplantation

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Bone marrow transplantation has the potential to improve the outcome of many indications other than cancer, but this is hampered by the associated complications. Myeloid progenitor cells (MP), which produce a transient engraftment

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The Clinical Outcome of Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) for Elderly Philadelphia Chromosome-Positive (Ph+) Acute Lymphoblastic Leukemia (ALL) in the Era of Tyrosine Kinase Inhibitor (TKI) : A Single Institute Experience

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